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Diagnostic Utility of miRNA Signature in Umbilical Cord Blood for Identification of Severe Neonatal Opioid Withdrawal Syndrome

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Background: Growing research recognizes the role of epigenetic mechanisms in neurodevelopmental disorders. Despite increasing prevalence of prenatal opioid exposure (POE) and Neonatal Opioid Withdrawal Syndrome (NOWS), current diagnostic approaches for identification of infants with severe NOWS rely on monitoring of symptoms of withdrawal. Circulating microRNAs (miRNAs) are small non-coding RNA molecules that intracellularly regulate RNA translation and are involved in cell-to-cell communication when released extracellularly.

Rationale/significance: There is an unmet need for novel laboratory approaches to proactively identify neonates at high-risk for NOWS development before the manifestation of withdrawal symptoms to improve observation, treatment, and outcomes for infants with POE.

Hypothesis: Given our previous research showing that circulating miRNAs could predict infant outcomes following ethanol exposure, we hypothesized that neonatal circulating miRNAs would have predictive value for identification of infants with severe NOWS shortly after birth, prior to symptom onset.

Results: Participants (n = 58) consisted of pregnant women receiving medications for opioid use disorder and their infants. NOWS severity was operationalized as the need for pharmacologic treatment and prolonged hospitalization (≥ 14 days). Cord blood miRNAs were assessed using semi-quantitative qRT-PCR arrays.

Expression of 5 miRNAs (miR-128-3p, miR-30c-5p, miR-421, let-7d-5p, miR-584-5p) predicted the need for pharmacologic treatment with high accuracy (area under the curve [AUC]: 0.94; sensitivity: 88.2%; specificity: 95.1%).

Discussion: These results demonstrate that miRNA-based tests, combined with key clinical indicators, can reliably and proactively risk-stratify opioid-exposed infants. Infant cord blood is a readily available biological matrix further attesting to the clinical utility of this diagnostic approach.